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=> d his

     (FILE 'HOME' ENTERED AT 14:30:58 ON 28 FEB 2007)

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L1         16963 S (CHEMILUMINESCENT OR LUMINOL OR LUCIGENIN OR LOPHINE OR ACRID
L2            27 S L1 AND (ENERGY ACCEPTOR OR PHOTOCHROMIC)
L3             5 S L2 AND (BIOLOGICALLY ACTIVE OR DRUG OR PHARMACEUTICAL)

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                 PHOTOCHROMIC)
L3             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 AND (BIOLOGICALLY ACTIVE OR
                 DRUG OR PHARMACEUTICAL)


=> d 1-5 bib abs
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L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:325744 CAPLUS
DN 142:397734
TI Preparation of prodrugs containing chemiluminescent and photochromic moieties for selective drug delivery
IN Mills, Randell L.; Wu, Guo-Zhang
PA USA
SO U.S. Pat. Appl. Publ., 199 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005080260	A1	20050414	US 2004-828558	20040421
PRAI US 2003-464354P	P	20030422		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method of synthesis of a chemical compound (I) having the formula A-B-C that may serve for applications such as drug delivery, where A is a chemiluminescent, moiety, B is a photochromic moiety, and C is a biol. active moiety where A-B-C may serve as a prodrug. Novel synthetic methods of the present invention to form the prodrug comprised the steps of (1) forming a benzophenone, (2) forming a diaryl ethylene, (3) attaching a phthalimide moiety to at least one of the aryl groups of the ethylene to form a phthalimide-ethylene conjugate, (4) condensing two ethylene-phthalimide conjugates to form a phthalimide-pentadiene conjugate, (5) converting the phthalimide to the phthalhydrazide by reaction with hydrazine to form a carrier compound according to the present invention, and (6) reacting the carrier compound with an nucleophilic moiety of the drug to form the corresponding prodrug. Alternatively the carrier can be prepared by using the halo-substituted diaryl ethylene to make the corresponding cationic leuco dye-like compound with known methods. The cationic compound then is protected by reacting with a nucleophile and coupled with the aminophathalimide by palladium-catalyzed amination to form the protected phthalimide-pentadiene conjugate. The latter is refluxed with hydrazine to convert its phthalimide to the phthalhydrazide and acidified to give the carrier. An addnl. aspect of the present invention relates to the use of these compds. as antiviral agents for the treatment of viral infections such as HIV and as anticancer agents for the treatment of cancers such as bowel, lung, and breast cancer.

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:356146 CAPLUS
DN 141:301244
TI Synthesis and evaluation of novel prodrugs of foscarnet and dideoxycytidine with a universal carrier compound comprising a chemiluminescent and a photochromic conjugate
AU Mills, Randell; Wu, Guo Zhang
CS Luminide Pharmaceutical Corporation, Cranbury, NJ, 08512, USA
SO Journal of Pharmaceutical Sciences (2004), 93(5), 1320-1336
CODEN: JPMSAE; ISSN: 0022-3549
PB Wiley-Liss, Inc.
DT Journal
LA English
AB To facilitate intracellular delivery of hydrophilic drugs, a general lipophilic carrier mol. was designed and synthesized. The carrier comprised a chemiluminescent-photochromic conjugate that potentiates diffusion across cell membranes to enhance intracellular uptake of the drug. The designed mechanism involves activation of the chemiluminescent moiety by intracellular oxygen free radicals and intermol. energy transfer of the excited state energy to the photochromic moiety to result in release of the drug to allow the desired pharmacol. effect to occur. Prodrugs of foscarnet and dideoxycytidine with several carriers caused suppression of a human immunodeficiency virus infection in human cultured macrophages that was up to five times more effective than the drug alone. Successful in vivo efficacy testing of prodrug has been accomplished by demonstrating the suppression of a retroviral infection of Friend leukemia virus in mice. Acute toxicity studies of the carrier indicated that it was nontoxic.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:613460 CAPLUS
DN 136:212591
TI Measurement of proteases using chemiluminescence-resonance-energy-transfer chimaeras between green fluorescent protein and aequorin
AU Waud, Jonathan P.; Fajardo, Alexandra Bermudez; Sudhaharan, Thankiah; Trimby, Andrew R.; Jeffery, Jinny; Jones, Ann; Campbell, Anthony K.
CS Department of Medical Biochemistry, Cardiff and Vale NHS Trust, Llandough Hospital, Penarth, CF64 2XX, UK
SO Biochemical Journal (2001), 357(3), 687-697
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
AB Homogeneous assays, without a separation step, are essential for measuring chemical events in live cells and for drug discovery screens, and are desirable for making measurements in cell exts. or clin. samples. Here we demonstrate the principle of chemiluminescence resonance energy transfer (CRET) as a homogeneous assay system, using two proteases as models, one extracellular (α-thrombin) and the other intracellular (caspase-3). Chimaeras were engineered with aequorin as the chemiluminescent energy donor and green fluorescent protein (GFP) or enhanced GFP as the energy acceptors, with a protease linker (6 or 18 amino acid residues) recognition site between the donor and acceptor. Flash chemiluminescent spectra (20-60 s) showed that the spectra of chimaeras matched GFP, being similar to that of luminous jellyfish, justifying their designation as "Rainbow" proteins. Addition of the protease shifted the emission spectrum to that of aequorin in a time- and dose-dependent manner. Separation of the proteolyzed fragments showed that the ratio of green to blue light matched the extent of proteolysis. The caspase-3 Rainbow protein was able to provide information on the specificity of caspases in vitro and in vivo. It was also able to monitor caspase-3 activation in cells provoked into apoptosis by staurosporine (1 or 2 μM). CRET can also monitor GFP fluor formation. The signal-to-noise ratio of our Rainbow proteins is superior to that of fluorescence resonance energy transfer, providing a potential platform for measuring agents that interact with the reactive site between the donor and acceptor.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:705748 CAPLUS
DN 123:296612
TI Prodrugs for selective drug delivery
IN Mills, Randell L.
PA USA
SO U.S., 76 pp. Cont.-in-part of U.S. Ser. No. 948,326, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5428163	A	19950627	US 1989-446439	19891204
	US 5773592	A	19980630	US 1995-450672	19950530
	US 6555663	B1	20030429	US 2000-733809	20001208
PRAI	US 1986-948326	B2	19861231		
	US 1988-175970	B2	19880331		
	US 1989-446439	A1	19891204		
	US 1995-450672	A1	19950530		
	US 1998-107338	B1	19980630		

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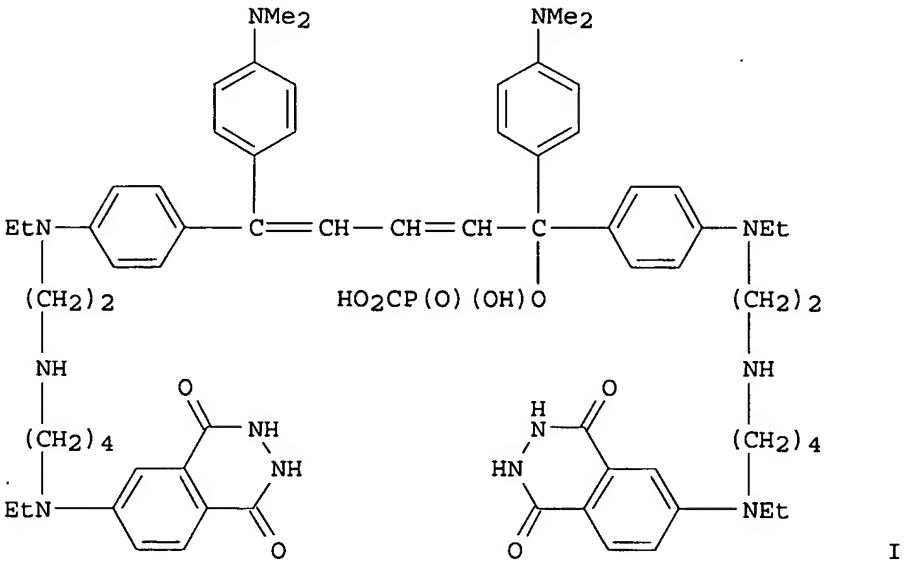

I

AB A class of pharmaceutical agents which react directly with electron carriers or with reactive species produced by electron transport to release a pharmacol. active mol. comprises (A) a functionality which is activatable by the environment [e.g. via an electron transfer functionality (D)] and capable of transferring energy from its excited state to (B) an energy acceptor which then achieves an excited state and relaxes through heterolytic cleavage of the covalent bond between B and (C), a drug moiety which is thereby released into the intracellular compartment. This type of prodrug, with structure ABC, DABC, ADBC, or AB(D)C, is designated a luminide. A is especially a chemiluminescent mol., e.g. a triarylmethane dye; B is a photochromic mol., e.g. any of several types of cationic dyes; C is a drug mol. with bleaching activity toward B or a

drug mol. conjugated to a bleaching nucleophilic group; D is a mol. able to undergo redox reactions. Thus, MTL J-1 (I), administered (10 μmol) to mice infected with Raucher spleen focus-forming virus (a model for HIV infection), prevented development of splenomegaly. I was prepared from p-dimethylaminobenzoic acid, N-ethyl-N-(2-chloroethyl)aniline, and N-(4-aminobutyl)-N-ethylisoluminol in several steps including dimerization.

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1990:111395 CAPLUS
DN 112:111395
TI Fluorogenic reaction between adenine derivatives and chloroacetaldehyde and its application to the determination of 9-(2-chloro-6-fluorobenzyl)adenine in human plasma
AU Matuszewski, Bogdan K.; Bayne, William F.
CS Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SO Analytica Chimica Acta (1989), 227(1), 189-202
CODEN: ACACAM; ISSN: 0003-2670
DT Journal
LA English
AB A sensitive (1 ng/mL) liquid chromatog. method with fluorescence detection is described for the determination of arprinocid and analogous compds. in human plasma. The method is based on chemical derivatization with chloroacetaldehyde to form highly fluorescent derivs. Extraction of the drug from plasma and separation of the derivative from the reaction mixture are accomplished by solid-phase extraction with 2 silica cartridges. The effects of pH, solvent, and concentration of the reagents of the efficiency of derivatization were studied. The assay in plasma was validated in the 1-50 ng/mL range. The fluorescent derivs. were synthesized and fully characterized. The derivs. were also found to be efficient as energy acceptors in the oxalate ester/H2O2 chemiluminescent system.

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 23, 2007 (20070223/UP).

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FILE COVERS 1907 - 28 Feb 2007  VOL 146 ISS 10
FILE LAST UPDATED: 27 Feb 2007  (20070227/ED)

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http://www.cas.org/infopolicy.html
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                 RANDELL L"/AU)
L5            16 SEA FILE=CAPLUS ABB=ON  PLU=ON  "WU GUO ZHANG"/AU
L6           108 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 OR L5
L7             4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND PRODRUG


=> d 1-4 bib abs
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L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:325744 CAPLUS
DN 142:397734
TI Preparation of prodrugs containing chemiluminescent and photochromic moieties for selective drug delivery
IN Mills, Randell L.; Wu, Guo-Zhang
PA USA
SO U.S. Pat. Appl. Publ., 199 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005080260	A1	20050414	US 2004-828558	20040421
PRAI	US 2003-464354P	P	20030422		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method of synthesis of a chemical compound (I) having the formula A-B-C that may serve for applications such as drug delivery, where A is a chemiluminescent, moiety, B is a photochromic moiety, and C is a biol. active moiety where A-B-C may serve as a prodrug. Novel synthetic methods of the present invention to form the prodrug comprised the steps of (1) forming a benzophenone, (2) forming a diaryl ethylene, (3) attaching a phthalimide moiety to at least one of the aryl groups of the ethylene to form a phthalimide-ethylene conjugate, (4) condensing two ethylene-phthalimide conjugates to form a phthalimide-pentadiene conjugate, (5) converting the phthalimide to the phthalhydrazide by reaction with hydrazine to form a carrier compound according to the present invention, and (6) reacting the carrier compound with an nucleophilic moiety of the drug to form the corresponding prodrug. Alternatively the carrier can be prepared by using the halo-substituted diaryl ethylene to make the corresponding cationic leuco dye-like compound with known methods. The cationic compound then is protected by reacting with a nucleophile and coupled with the aminophathalimide by palladium-catalyzed amination to form the protected phthalimide-pentadiene conjugate. The latter is refluxed with hydrazine to convert its phthalimide to the phthalhydrazide and acidified to give the carrier. An addnl. aspect of the present invention relates to the use of these compds. as antiviral agents for the treatment of viral infections such as HIV and as anticancer agents for the treatment of cancers such as bowel, lung, and breast cancer.

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:356146 CAPLUS
DN 141:301244
TI Synthesis and evaluation of novel prodrugs of foscarnet and dideoxycytidine with a universal carrier compound comprising a chemiluminescent and a photochromic conjugate
AU Mills, Randell; Wu, Guo Zhang
CS Luminide Pharmaceutical Corporation, Cranbury, NJ, 08512, USA
SO Journal of Pharmaceutical Sciences (2004), 93(5), 1320-1336
CODEN: JPMSAE; ISSN: 0022-3549
PB Wiley-Liss, Inc.
DT Journal
LA English
AB To facilitate intracellular delivery of hydrophilic drugs, a general lipophilic carrier mol. was designed and synthesized. The carrier comprised a chemiluminescent-photochromic conjugate that potentiates diffusion across cell membranes to enhance intracellular uptake of the drug. The designed mechanism involves activation of the chemiluminescent moiety by intracellular oxygen free radicals and intermol. energy transfer of the excited state energy to the photochromic moiety to result in release of the drug to allow the desired pharmacol. effect to occur. Prodrugs of foscarnet and dideoxycytidine with several carriers caused suppression of a human immunodeficiency virus infection in human cultured macrophages that was up to five times more effective than the drug alone. Successful in vivo efficacy testing of prodrug has been accomplished by demonstrating the suppression of a retroviral infection of Friend leukemia virus in mice. Acute toxicity studies of the carrier indicated that it was nontoxic.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:923643 CAPLUS
DN 136:42881
TI Prodrugs for selective drug delivery comprising a photochromic moiety and thermochromic moiety
IN Mills, Randell L.
PA USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095944	A2	20011220	WO 2001-US18869	20010612
	WO 2001095944	A3	20020808		
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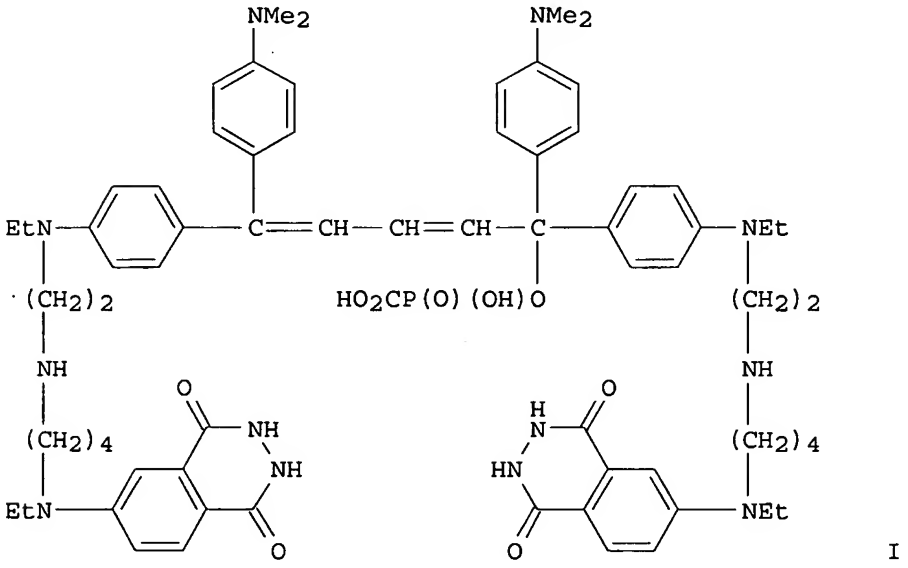
	AU 2001066861	A5	20011224	AU 2001-66861	20010612
	US 2003228644	A1	20031211	US 2002-316989	20021210
	US 7015352	B2	20060321		
PRAI	US 2000-211036P	P	20000612		
	WO 2001-US18869	W	20010612		

AB Prodrug compds. are disclosed capable of permeating a desired biol. compartment and releasing a biol. active mol. in active form to effect a therapeutic functional change in the compartment to which it is introduced. An exemplary luminide is 1-phosphonoformate,1,5,di-(p-N-ethyl-N-ethylaminophenyl)-1,5-bis-(p-N,N-dimethylaniline)-1,3-pentadiene.

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:705748 CAPLUS
DN 123:296612
TI Prodrugs for selective drug delivery
IN Mills, Randell L.
PA USA
SO U.S., 76 pp. Cont.-in-part of U.S. Ser. No. 948,326, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5428163	A	19950627	US 1989-446439	19891204
	US 5773592	A	19980630	US 1995-450672	19950530
	US 6555663	B1	20030429	US 2000-733809	20001208
PRAI	US 1986-948326	B2	19861231		
	US 1988-175970	B2	19880331		
	US 1989-446439	A1	19891204		
	US 1995-450672	A1	19950530		
	US 1998-107338	B1	19980630		

GI



I

AB A class of pharmaceutical agents which react directly with electron carriers or with reactive species produced by electron transport to release a pharmacol. active mol. comprises (A) a functionality which is activatable by the environment [e.g. via an electron transfer functionality (D)] and capable of transferring energy from its excited state to (B) an energy acceptor which then achieves an excited state and relaxes through heterolytic cleavage of the covalent bond between B and (C), a drug moiety which is thereby released into the intracellular compartment. This type of prodrug, with structure ABC, DABC, ADBC, or AB(D)C, is designated a luminide. A is especially a chemiluminescent mol., e.g. a triarylmethane dye; B is a photochromic mol., e.g. any of several types of cationic dyes; C is a drug mol. with bleaching activity toward B or a drug mol. conjugated to a bleaching nucleophilic group; D is

a mol. able to undergo redox reactions. Thus, MTL J-1 (I), administered (10 μmol) to mice infected with Raucher spleen focus-forming virus (a model for HIV infection), prevented development of splenomegaly. I was prepared from p-dimethylaminobenzoic acid, N-ethyl-N-(2-chloroethyl)aniline, and N-(4-aminobutyl)-N-ethylisoluminol in several steps including dimerization.

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                OR LOPHINE OR ACRIDINIUM OR PHTHALHYDRAZIDE)
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                PHARMACEUTICAL)
                D QUE L3 STAT
                D 1-5 BIB ABS

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                E WU GUO ZHANG/AU
L5           16 SEA ABB=ON  PLU=ON  "WU GUO ZHANG"/AU
L6          108 SEA ABB=ON  PLU=ON  L4 OR L5
L7            4 SEA ABB=ON  PLU=ON  L6 AND PRODRUG
                D QUE L7 STAT
                D 1-4 BIB ABS


     FILE HOME

     FILE CAPLUS

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     LAST RELOADED: Feb 23, 2007 (20070223/UP).

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                OR #PHTHALIC)


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L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:325744 CAPLUS
DN 142:397734
TI Preparation of prodrugs containing chemiluminescent and photochromic moieties for selective drug delivery
IN Mills, Randell L.; Wu, Guo-Zhang
PA USA
SO U.S. Pat. Appl. Publ., 199 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005080260	A1	20050414	US 2004-828558	20040421
PRAI US 2003-464354P	P	20030422		

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L3            5 SEA ABB=ON  PLU=ON  L2 AND (BIOLOGICALLY ACTIVE OR DRUG OR
                PHARMACEUTICAL)
                D QUE L3 STAT
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     FILE 'CAPLUS' ENTERED AT 14:36:44 ON 28 FEB 2007
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L5           16 SEA ABB=ON  PLU=ON  "WU GUO ZHANG"/AU
L6          108 SEA ABB=ON  PLU=ON  L4 OR L5
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                D BIB ABS


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